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How to test very soft biological tissues in extension?

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Abstract

Mechanical properties of very soft tissues, such as brain, liver and kidney, until recently have largely escaped the attention of researchers because these tissues do not bear mechanical loads. However, developments in Computer–Integrated and Robot–Aided Surgery — in particular, the emergence of automatic surgical tools and robots — as well as advances in Virtual Reality techniques, require closer examination of the mechanical properties of very soft tissues and, ultimately, the construction of corresponding, realistic mathematical models. A body of knowledge about mechanical properties of very soft tissues, assembled in recent years, has been almost exclusively based on the results of compression, indentation and impact tests. There are no results of tensile tests available. This state of affairs, in the author's opinion, is caused by the lack of analytical solution relating a measured quantity — machine head displacement — to strain in simple extension experiments of cylindrical samples with low aspect ratio. In the paper this important solution is presented. The theoretical solution obtained is valid for isotropic, incompressible materials for moderate deformations (< 30%) when it can be assumed that planes initially perpendicular to the direction of applied extension remain plane. Two astonishing results are obtained: (i) deformed shape of a cylindrical sample subjected to uniaxial extension is independent on the form of constitutive law, (ii) vertical extension in the plane of symmetry λ_z is proportional to the total change of height for strains as large as 30%. The importance and relevance of these results to testing procedures in Biomechanics is highlighted.

Keywords: Soft tissue; Mechanical properties; Mathematical modelling; Tension experiment

1. Introduction

Mechanical properties of living tissues form a central subject in Biomechanics. Recent developments in robotics technology, especially the emergence of automatic surgical tools and robots (e.g. Brett et al., 1995) as well as advances in virtual reality techniques (Burdea, 1996) provide immediate and important applications to research into the mechanical properties of very soft tissues, such as brain, liver and kidney. These tissues have been largely neglected before because they do not bear mechanical loads. Mathematical models of brain tissue mechanical properties may find application, for example, in a surgical robot control system where the prediction of deformation is needed (Miller and Chinzei, 1995, 2000); surgical operation planning and surgeon training systems based on the virtual reality techniques (Burdea, 1996 and references cited therein) where *force feedback* is needed; and in *registration* (Lavallée, 1995) where knowledge of local deformation is required.

There is a wealth of information available in the literature about the mechanical properties of brain tissue in-vitro (Ommaya, 1968; Estes and McElhaney, 1970; Galford and McElhaney, 1970; Pamidi and Advani, 1978; Bilston et al., 1997; Donnelly and Medige, 1997; Miller and Chinzei, 1997). Some information on liver and kidney tissue mechanical properties has also been published (e.g. Melvin et al., 1973; Farshad et al., 1998, 1999; Miller, 2000). However, the experimental results available in literature are limited to compression, indentation and impact tests and to a lesser extent, torsional tests. To the best of the author's knowledge, there are no results in the literature concerning very soft tissue properties in tension. Why is that? The author believes that, besides technical problems with conducting extension tests on brain and other soft tissues, the main reason is that the analytical relation between the

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tensile stress machine head displacement and strain is not known for cylindrical samples with a low aspect ratio.

In this paper I develop the rigorous mathematical description of the deformation in the uniaxial extension experiment and derive the relation between the machine head displacement and strain needed for the constitutive law identification. It is claimed that the results obtained allow the analysis of uniaxial extension experiments performed on low aspect ratio cylindrical samples of soft biological tissues in an analogous way to that routinely used in the unconfined compression.

2. Extension experiment set-up

Typically, in experiments on brain tissue cylindrical samples of diameter $\sim$30 mm and height $\sim$10 mm are used (Miller and Chinzei, 1997). Steel pipe (30 mm diameter) with sharp edges is used to cut the samples. The faces of the cylindrical brain specimens are smoothed manually, using a surgical scalpel.

Uniaxial tension of brain (or other very soft tissue) can be performed in a testing stand sketched in Fig. 1. This particular geometry is dictated by the difficulties in attaching faces of cylindrical specimens to platens of the stress–strain machine. Probably the best choice is to use surgical glue. It is important to note here that it is very difficult (if not impossible) to extract elongated samples of very soft tissues to be tested in extension using standard engineering procedures.

The testing apparatus should be able to move the machine head within large range of velocities (to simulate strain rates typical to impact, surgical or quasi-static conditions) and measure accurately small (fractions of a Newton) vertical forces.

3. Theoretical analysis of extension experiment

In extension experiment the kinematics of the deformation is complex, prohibiting the existence of the exact analytical solution for the deformation of the sample for any realistic constitutive law chosen to describe tissue mechanical properties. This, in the author' opinion, is one of the reasons why there are no extension results for soft tissues published in the biomechanics literature. However, with a few reasonable assumptions an approximate solution can be found.

I consider a circular cylinder bonded between two rigid end-plates (Fig. 2). The disc of radius R and height $2H$ in undeformed state is strained to the final height $2h$ by uniform vertical motion of the end-plates. For the coordinate system in the unstrained state Cartesian coordinates $\{X,Y,Z\}$ are taken. The Cartesian coordinate system $\{x, y, z\}$ for deformed body is chosen to coincide with the system $\{X,Y,Z\}$.

In the theoretical derivation the following simplifying assumptions are needed:

Material properties

(a) Material is incompressible,
(b) Material is isotropic.

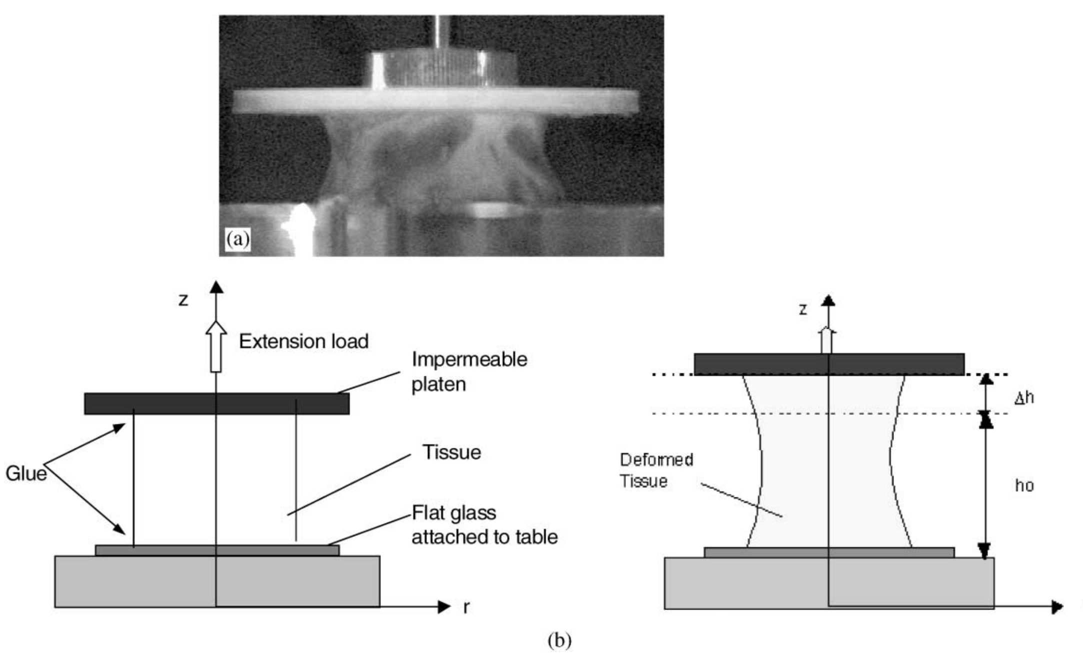

Fig. 1. (a) Swine brain tissue sample subjected to extension. Zero-Time jelly (cyanoacrylate type), surgical glue from Cemedine (Japanese company) was used to attach sample to the top and bottom platens of the stress machine. (b) Sketch of the experimental set-up. Δh and vertical force are measured.

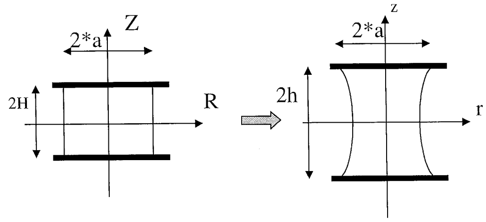

Fig. 2. Description of deformation in extension experiment: undeformed (left) and deformed (right) configuration. The fixed radius of cylindrical sample at the top and bottom is denoted as "a". In the undeformed configuration it is equal to the radius of the sample.

Deformation

(c) Deformation is moderate ($<30\%$, as compared to deformations exceeding 100%, common in rubber research), so that any polynomial strain energy function can be reasonably approximated by its first-order terms,
(d) Planes perpendicular to the direction of the applied force remain plane — common and reasonable assumption following from allowing only moderate deformation,
(e) Force and moment resultants vanish on every portion of the free surface.

It is important to note that nothing is assumed about the true form of the energy function.

Under the assumption that the planes perpendicular to the direction of the applied force remain plane the deformation of the specimen can be described as follows:

$$z = g[Z], \tag{1}$$

$$r = Rf[Z] \Rightarrow x = Xf[Z], \tag{2}$$

$$y = Yf[Z]. \tag{3}$$

Eqs. (1)–(3) follow from symmetry.

Very soft tissues are most often assumed to be incompressible (see e.g. Pamidi and Advani, 1978; Walsh and Schettini, 1984; Sahay et al., 1992; Mendis et al., 1995; Miller and Chinzei, 1997; Farshad et al., 1998; Miller, 1999, 2000). The author tried to detect a departure from incompressibility assumption for brain tissue using laser measurement and image analysis techniques — unsuccessfully (Chinzei and Miller, 1996). Also, during compression experiments (Miller and Chinzei, 1997) the author did not notice any fluid being squeezed out from brain tissue samples. Therefore, I conclude that incompressibility assumption can be confidently used. The incompressibility of the tissue should not be confused with apparent compressibility of an organ as a whole, observed e.g. by Guillaume et al. (1997) for brain in hypergravity experiments.

The incompressibility condition gives

$$f^2[Z] * g'[Z] = 1 \tag{4}$$

Deformation gradient is

$$\mathbf{F} = \begin{bmatrix} f[Z] & 0 & Xf'[Z] \\ 0 & f[Z] & Yf'[Z] \\ 0 & 0 & g'[Z] \end{bmatrix}. \tag{5}$$

In the plane of symmetry, $Z = 0$, off-diagonal components of the deformation gradient vanish. This is a very important observation — the deformation in the plane of symmetry is orthogonal.

$$\mathbf{F}(X, Y, 0) = \begin{bmatrix} \lambda_z^{1/2} & 0 & 0 \\ 0 & \lambda_z^{1/2} & 0 \\ 0 & 0 & \lambda_z \end{bmatrix}, \tag{6}$$

where λ_z is a stretch in vertical direction (Fig. 2b):

$$\lambda_z = g'(0) = f(0)^{-2}. \tag{7}$$

In such case, one can compute the only non−zero Lagrange stress component from the simple formula:

$$T_{zz} = \frac{\partial W}{\partial \lambda_z}. \tag{8}$$

In practice, to evaluate the above equation one has to relate extension in the plane of symmetry to the applied movement of the end-plate (machine head). This can be, in principle, achieved by examination of camera images of the experiment. The relative change in specimen radius in the plane of symmetry r/R can be measured for a given relative displacement of the end-plate h/H. Using the incompressibility condition (Eqs. (4) or (7)) extension in vertical direction can be uniquely determined. Unfortunately, basing on the extensive experience with brain tissue I conclude that this procedure is difficult to reliably apply in practice mostly due to too large pixel size and departures from exact cylindrical shape of samples.

A different and more reliable method is proposed in this study. In the reminder of this section I will show that it is possible to relate the total change of height h/H to the extension in the plane of symmetry λ_z without the reference to the particular form of energy function W, which can be, in full generality, a function of deformation, history of deformation and time explicitly.

The problem of finding the deformation of the tissue subject to the displacement of the machine head can be described by equation of equilibrium, constitutive law and boundary conditions. The equation of equilibrium, using Einstein's summation convention is

$$\mathbf{t}^{ij}_{j} = 0, \tag{9}$$

where $\mathbf{t}$ denotes Cauchy stress and coma indicates covariant differentiation with respect to deformed configuration.

Very soft tissues do not bear mechanical loads and do not exhibit directional structure. Therefore, they may be assumed to be initially isotropic (see e.g. Pamidi and Advani, 1978; Walsh and Schettini, 1984; Sahay et al., 1992; Mendis et al., 1995; Miller and Chinzei, 1997; Farshad et al., 1998; Miller, 1999, 2000). The most general form of the constitutive law for incompressible, *isotropic* materials (the most general isotropic tensor function) is

$$\mathbf{t} = 2\frac{\partial W}{\partial I_1}\mathbf{B} - 2\frac{\partial W}{\partial I_2}\mathbf{B}^{-1} - p\mathbf{g}, \tag{10}$$

where $\mathbf{B}=\mathbf{F}\ \mathbf{F}^{\mathrm{T}}$ is a Left Cauchy–Green strain tensor, $I_1=$ Trace[**B**], $I_2 = 1/2\ (I_1^2-\mathrm{Trace}[\mathbf{B}^2])$ are first and second strain invariants, p is a scalar hydrostatic pressure and $\mathbf{g}$ is a metric tensor.

The boundary conditions are (see Fig. 2)

- glue : on $Z = +H$ or $-H \Rightarrow r = R$ and $z = +h$ or $-h$, (11)
- surface free from forces and moments on $R = a$. (12)

It should be noted here that in derivation of the relation between machine head displacement h/H and the stretch in the plane of symmetry λ_z the force boundary condition (12) is not used.

It can be immediately seen that when the energy function W is allowed to take any functional form, the coefficients $\partial W/\partial I_1$, $\partial W/\partial I_2$ in Eq. (10) will be functions of position and possibly of deformation as well. After the substitution to the equation of equilibrium (9) the formulas, as a result of covariant differentiation, would expand enormously leaving no hope of finding analytical solutions whatsoever. However, any complicated, non-linear energy function can be expanded in polynomial series around the unloaded (unstrained) configuration. The deformation encountered in very soft tissue biomechanics never exeeds strain levels of about 30%. Beyond this limit tissues suffer permanent damage. So that, for such a moderate range of deformations it is reasonable to approximate the energy function by the polynomial expansion truncated after the linear term:

$$W = C_1(I_1 - 3) + C_2(I_2 - 3). \tag{13}$$

This, so called Mooney–Rivlin form of energy function has been frequently used in rubber deformation modelling. The physical meaning of constants C_1, C_2 in the limit of infinitesimal deformation is: $\mu/2 = C_1 + C_2$, where μ is the shear modulus. For such a choice of the energy function, the coefficients $\partial W/\partial I_1 = C_1$, $\partial W/\partial I_2 = C_2$ in Eq. (10) are just numbers and the substitution to Eq. (9) yields a managable set of partial differential equations (in cylindrical co-ordinates):

$$\frac{\partial p}{\partial R} = -2\frac{\partial W}{\partial I_1}R^*f^*f'' - 2\frac{\partial W}{\partial I_2}R^*f^2[f^*f'' + (f')^2], \tag{14}$$

$$\frac{\partial p}{\partial \theta} = 0, \tag{15}$$

$$\frac{\partial p}{\partial Z} = -2\frac{\partial W}{\partial I_1}\left\{R^{2*}f^*f'' - \frac{2f'}{f^v}\right\} - 2\frac{\partial W}{\partial I_2}\left\{R^{2*}f^*f'[f^*f'' + (f')^2] - \frac{2f'}{f'''}\right\}. \tag{16}$$

4. Results

By differentiating Eq. (14) with respect to Z, Eq. (16) with respect to R, and equating the results one obtains a single ordinary differential equation for the shape of the deformed sample $f\,(Z)$:

$$\frac{\partial W}{\partial I_1}\frac{\mathrm{d}}{\mathrm{d}Z}\left(\frac{f''}{f}\right) + \frac{\partial W}{\partial I_2}\frac{\mathrm{d}^3}{\mathrm{d}Z^3}\left(\frac{1}{2}f^2\right) = 0. \tag{17}$$

Unfortunately, the solutions of Eq. (17) can be found only in the implicit form:

$$z + \frac{\mathrm{EllipticE}\left[\mathrm{ArcSin}\left[\frac{f\,[z]}{f\,[0]}\right], -\frac{C_2 f\,[0]^2}{C_1}\right] f\,[0]\sqrt{\frac{f[0]^2 - f[z]^2}{f[0]^2}}}{\sqrt{\frac{(C_1 + C_2)\ \mathrm{Const}\,1(-f[0]^2 + f[z]^2}{C_1 + C_2 f[z]^2}}\sqrt{\frac{C_1 + C_2 f[z]^2}{C_1}}} = \mathrm{Const2} \tag{18}$$

$$-z + \frac{\mathrm{EllipticE}\left[\mathrm{ArcSin}\left[\frac{f\,[z]}{f\,[0]}\right], -\frac{C_2 f[0]^2}{C_1}\right] f\,[0]\sqrt{\frac{f\,[0]^2 - f\,[z]^2}{f\,[0]^2}}}{\sqrt{\frac{(C_1 + C_2)\ \mathrm{Const}\,1\,(-f\,[0]^2 + f\,[z]^2)}{C_1 + C_2 f[z]^2}}\sqrt{\frac{C_1 + C_2 f[z]^2}{C_1}}} = \mathrm{Const2} \tag{19}$$

In above equations EllipticE denotes the elliptic integral of the second kind. Two different solutions correspond to the compression and extension cases respectively. The solutions contain only two integration constants Const1 and Const2 because the condition that the function $f[Z]$ is even – $f'[Z = 0] = 0$ – is already included. As can be immediately seen, the task of incorporating the boundary conditions (11) into the implicit solutions for the function $f(Z)$ is very difficult. It will not be attempted in this paper. However, it is known from the long experience of the rubber industry (see e.g. Rivlin, 1984; Treloar, 1975) that the following cases constitute two extremes in material behaviour:

- Neo-Hookean material $\Rightarrow W = C_1(I_1 - 3)$, $\mu/2 = C_1$
- Extreme-Mooney material $\Rightarrow W = C_2(I_2 - 3)$, $\mu/2 = C_2$

For moderate deformations, real materials fall somewhere in between these two extremes. Klingbeil and Shield (1966) found the solutions for these extreme cases:

For Neo-Hookean material $\Rightarrow W = C_1(I_1 - 3)$; $\mu/2 = C_1$

$$\frac{h}{H} = \frac{\sqrt{1-\lambda_z^{-1}}}{\lambda_z^{-1}\,\mathrm{ArcSech}(\lambda_z^{-1/2})}, \tag{20}$$

$$f(Z) = \lambda_z^{-1/2}\,\mathrm{Cosh}\left\{\frac{\mathrm{ArcSech}[\lambda_z^{-1/2}]}{H} Z\right\} \tag{21}$$

and for Extreme-Mooney material $\Rightarrow W = C_2(I_2 - 3)$; $\mu/2 = C_2$,

$$\frac{h}{H} = \frac{\mathrm{ArcCos}(\lambda_z^{-1/2})}{\lambda_z^{-1/2}\sqrt{1-\lambda_z^{-1}}}, \tag{22}$$

$$f(Z) = \lambda_z^{-1/2}\left\{1 + \left[\frac{\sqrt{1-\lambda_z^{-1}}\,Z}{H\lambda_z^{-1/2}}\right]^2\right\}^{1/2}. \tag{23}$$

To plot the deformed shapes for both cases for a given displacement of the machine head h/H one has to compute numerically the vertical stretch in the plane of symmetry λ_z from Eqs. (20) and (22), and substitute to Eqs. (21) and (23), respectively. Fig. 3 shows the comparison of the deformed shape for different extension levels for these two extreme cases.

It can be seen that despite apparent differences in the form of equations the actual deformed shaped is almost the same. The maximum difference in radius for $h/H = 1.3$ does not exceed 1%. From the perspective of testing biological materials, which inherently exhibit large variability of mechanical properties (see e.g. Estes and McElhaney, 1970; Miller and Chinzei, 1997 for brain; Melvin et al., 1973, Farshad et al., 1998, 1999, for liver and kidney), this difference in shape, and the resulting difference in the cross-section area are negligible. For practical purposes it can be concluded that the deformed shape of the cylindrical sample of incompressible biological material is insensitive to the form of the constitutive law defining its mechanical properties.

To further strengthen the argument, the boundary value problem consisting of Eqs. (4) and (17), subject to boundary conditions $f(Z=H)=1$, $f'(Z=0)=0$, $g(Z=0)=0$, $g(Z=H)=h/H$, was solved numerically (by standard shooting method) for various ratios C_1/C_2. As expected, results for the shape, $f(Z)$, fall between the extremes of Fig. 3.

When the applied strain $e = h/H - 1$ is small, so that the second and higher powers of e are negligible, the displacements are

$$\frac{r}{R} = f(Z) = 1 - \frac{3}{4}e\left(1 - \frac{Z^2}{H^2}\right), \tag{24}$$

$$z = g(Z) = Z\left(1 + \frac{3}{2}e\left(1 - \frac{Z^2}{3H^2}\right)\right). \tag{25}$$

Fig. 4 presents, for the two extreme cases, the relationship between the vertical stretch in the plane of

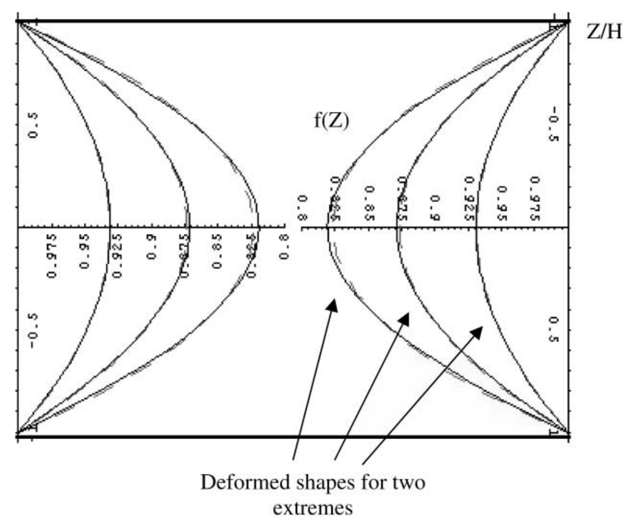

Fig. 3. Deformed shapes of samples made of Neo-Hookean (dashed line) and Extreme-Mooney (solid line) materials for $h/H = 1.1$, 1.2 and 1.3 — for practical purposes deformed shapes for the two extreme cases are the same. Numerically calculated shapes for various ratios C_1/C_2 (not shown) fall between the extremes shown.

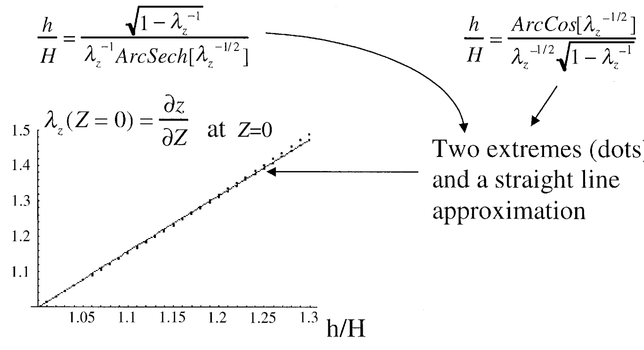

Fig. 4. Linear (for practical purposes) relationship between the measured machine head movement h/H and the vertical stretch in the plane of symmetry $\lambda_z(Z=0)$ for samples made of Neo-Hookean and Extreme-Mooney materials.

symmetry λ_z and the displacement of the machine head h/H, Eqs. (20) and (22).

Even though Eqs. (20) and (22) look complicated they really describe, to high accuracy, a linear relationship. The vertical stretch in the plane of symmetry is proportional to the change in total hight, at least for h/H between 1 and 1.3.

$$\lambda_z(Z=0) = K\left(\frac{h}{H}-1\right), \quad K = 1.583. \tag{26}$$

5. Discussion and conclusions

Two theoretical results presented in this paper have important implications for testing in biomechanics of very soft tissues. As shown above, in a uniaxial extension experiment, in the plane of symmetry $Z = z = 0$ (see Fig. 2) the orthogonal state of deformation can be assumed. This state of deformation can be described, as in the case of the unconfined compression experiment (Miller and Chinzei, 1997), by a diagonal deformation gradient:

$$\mathbf{F}(Z=0) = \begin{bmatrix} f(0) & 0 & 0 \\ 0 & f(0) & 0 \\ 0 & 0 & g'(0) \end{bmatrix} = \begin{bmatrix} \lambda_z^{-1/2} & 0 & 0 \\ 0 & \lambda_z^{-1/2} & 0 \\ 0 & 0 & \lambda_z \end{bmatrix} \tag{27}$$

Therefore, the results of the uniaxial extension of cylindrical biological specimens can be analysed in analogous way to that used in the unconfined compression:

Unconfined compression

$$\Rightarrow \lambda_z(Z=(0) = \frac{h}{H}. \tag{28}$$

Uniaxial extension (see Fig. 1)

$$\Rightarrow \lambda_z(Z=(0)-1 = K\left(\frac{h}{H}-1\right), \quad K = 1.583. \tag{29}$$

To test how the properties of tissue change with the speed of loading (strain rate) one would like to conduct series of experiments for various, but constant, nominal strain rates. Since λ_z is linearly related to h/H, constant velocities of the machine head $h/H=$ constant translate to constant stretch rates in the plane of symmetry $\dot{\lambda}_z(Z=0)$. This is an important feature which allows Eq. (8) to be resolved analytically even for complicated forms of potential function W used, e.g. in hyper-viscoelastic constitutive laws for brain tissue (Miller and Chinzei, 1997; Miller,1999):

$$W = \int_0^t \left\{ \sum_{i+j=1}^{N} \left[C_{ij0}\left(1 - \sum_{k=1}^{n} g_k\left(1 - \mathrm{e}^{-(t-\tau/\tau_k)}\right)\right)\right] \frac{\mathrm{d}}{\mathrm{d}\tau}\left[(I_1-3)^i (I_2-3)^j\right] \right\} \mathrm{d}\tau \tag{30}$$

where τ_k are characteristic times, g_k are relaxation coefficients, N is the order of polynomial in strain invariants (as a result of the assumption of the brain tissue initial isotropy the energy depends on the histories of strain invariants only) used for strain energy function description and I_1, I_2 are strain invariants.

Even for such a complicated form of the energy function formula (8) for Lagrange stress, in the case of the unconfined compression, can be evaluated analytically (Miller, 1999). As shown in this paper, due to the linear relationship between λ_z and h/H, the same solution (with the correction by a constant $K = 1.583$) can be used in analysing extension experiments.

When applying the results of this paper one must be aware of the simplifying assumptions used in the derivation. In particular, the solutions obtained are valid only for isotropic, incompressible materials. Thus, they cannot be used for load bearing tissues, which usually exhibit directional properties. Also, in this paper only moderate stretches were investigated and no assurance can be given for the validity of results for deformations (h/H) beyond 30%.

In constitutive modelling of brain and other soft tissues the assumption of the equality of energies of the deformation and the reciprocal deformation has often been used (for discussion see Mooney, 1940; Miller and Chinzei, 1997, Miller, 1999, 2000). This assumption has never been tested. The results presented in this paper open the possibility of simple testing of very soft tissues in extension and developing constitutive models with larger range of applicability. The assumption of the equality of the energy of the deformation and the energy of the reciprocal deformation will be proved or disproved in the process.

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